
The clinical applications of genome editing in HIV.

Journal:	Blood
Publication Year:	2016
Authors:	Cathy X Wang, Paula M Cannon
PubMed link:	27053530
Funding Grants:	Site-specific gene editing in hematopoietic stem cells as an anti-HIV therapy

Public Summary:

HIV/AIDS has long been at the forefront of the development of gene- and cell-based therapies. Although conventional gene therapy approaches typically involve the addition of anti-HIV genes to cells using semirandomly integrating viral vectors, newer genome editing technologies based on engineered nucleases are now allowing more precise genetic manipulations. The possible outcomes of genome editing include gene disruption, which has been most notably applied to the CCR5 coreceptor gene, or the introduction of small mutations or larger whole gene cassette insertions at a targeted locus. Disruption of CCR5 using zinc finger nucleases was the first-in-human application of genome editing and remains the most clinically advanced platform, with 7 completed or ongoing clinical trials in T cells and hematopoietic stem/progenitor cells (HSPCs). Here we review the laboratory and clinical findings of CCR5 editing in T cells and HSPCs for HIV therapy and summarize other promising genome editing approaches for future clinical development. In particular, recent advances in the delivery of genome editing reagents and the demonstration of highly efficient homology-directed editing in both T cells and HSPCs are expected to spur the development of even more sophisticated applications of this technology for HIV therapy.

Scientific Abstract:

HIV/AIDS has long been at the forefront of the development of gene- and cell-based therapies. Although conventional gene therapy approaches typically involve the addition of anti-HIV genes to cells using semirandomly integrating viral vectors, newer genome editing technologies based on engineered nucleases are now allowing more precise genetic manipulations. The possible outcomes of genome editing include gene disruption, which has been most notably applied to the CCR5 coreceptor gene, or the introduction of small mutations or larger whole gene cassette insertions at a targeted locus. Disruption of CCR5 using zinc finger nucleases was the first-in-human application of genome editing and remains the most clinically advanced platform, with 7 completed or ongoing clinical trials in T cells and hematopoietic stem/progenitor cells (HSPCs). Here we review the laboratory and clinical findings of CCR5 editing in T cells and HSPCs for HIV therapy and summarize other promising genome editing approaches for future clinical development. In particular, recent advances in the delivery of genome editing reagents and the demonstration of highly efficient homology-directed editing in both T cells and HSPCs are expected to spur the development of even more sophisticated applications of this technology for HIV therapy.

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